10/764,676

~~10/479,080~~

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN
NEWS	24	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	25	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	26	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	27	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	28	MAR 22	PATDPASPC - New patent database available
NEWS	29	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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 NEWS HOURS     STN Operating Hours Plus Help Desk Availability
 NEWS INTER     General Internet Information
 NEWS LOGIN     Welcome Banner and News Items
 NEWS PHONE     Direct Dial and Telecommunication Network Access to STN
 NEWS WWW       CAS World Wide Web Site (general information)

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  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 20:19:30 ON 23 MAR 2005

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 20:19:40 ON 23 MAR 2005
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   22 MAR 2005  HIGHEST RN 847018-75-1
DICTIONARY FILE UPDATES:  22 MAR 2005  HIGHEST RN 847018-75-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*********************************************************************
*                                                                   *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                   *
*********************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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Uploading C:\Program Files\Stnexp\Queries\10479080.str
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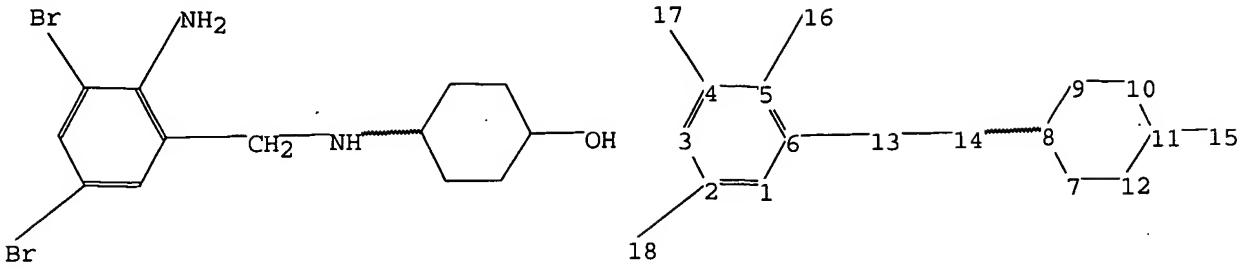
~~10/479,080~~ 10/764,676



chain nodes :
13 14 15 16 17 18
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
2-18 4-17 5-16 6-13 8-14 11-15 13-14
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
5-16 8-14 11-15
exact bonds :
2-18 4-17 6-13 7-8 7-12 8-9 9-10 10-11 11-12 13-14
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 7 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

L1 STRUCTURE UPLOADED

=> s l1 ful
FULL SEARCH INITIATED 20:20:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 142 TO ITERATE

100.0% PROCESSED 142 ITERATIONS 39 ANSWERS
SEARCH TIME: 00.00.01

L2 39 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	161.33	161.54

FILE 'CAPLUS' ENTERED AT 20:20:17 ON 23 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 23 Mar 2005 VOL 142 ISS 13
FILE LAST UPDATED: 22 Mar 2005 (20050322/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l2
L3          501 L2

=> s l3 and (lipid or lipoic acid)
         249520 LIPID
         201149 LIPIDS
         311320 LIPID
                (LIPID OR LIPIDS)
           3317 LIPOIC
        3953527 ACID
        1469296 ACIDS
        4429774 ACID
                (ACID OR ACIDS)
           3275 LIPOIC ACID
                (LIPOIC(W)ACID)
L4            24 L3 AND (LIPID OR LIPOIC ACID)

=> d l4 ibib hitstr abs 1-24

L4   ANSWER 1 OF 24  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:965034  CAPLUS
DOCUMENT NUMBER:          141:400958
TITLE:                    Drug formulations with methacrylic
                          acid-methylacrylate-ethylacrylate-butylmethacrylate
                          copolymer containing coating or matrix
INVENTOR(S):              Petereit, Hans-Ulrich; Meier, Christian; Schultes,
                          Klaus
PATENT ASSIGNEE(S):       Roehm G.m.b.H. & Co. K.-G., Germany
SOURCE:                   PCT Int. Appl., 47 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2004096185         A1    20041111    WO 2004-EP2061          20040302
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

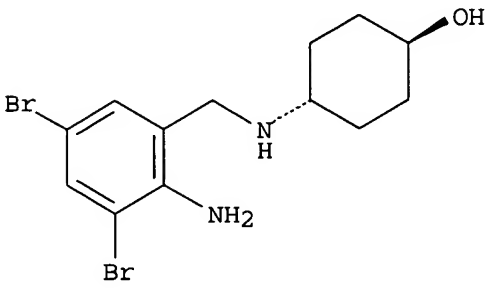
DE 10319458	A1	20041118	DE 2003-10319458	20030429
EP 1496870	A1	20050119	EP 2004-716230	20040302

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

PRIORITY APPLN. INFO.:	DE 2003-10319458	A 20030429
	WO 2004-EP2061	W 20040302

IT **18683-91-5**, Ambroxol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug formulations with methacrylic acid-methylacrylate-ethylacrylate-butylmethacrylate copolymer containing coating or matrix)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



AB The invention relates to a method for producing a coated dosage form or a dosage form in the form of a matrix containing an active substance. The dosage form is produced by processing a copolymer that contains a pharmaceutical active substance, an optional core and/or pharmaceutically conventional aggregates in a manner known per se by melting, injection-molding, extrusion, wet granulation, casting, dipping, spreading, spraying or compaction to give a coated dosage form and/or to give a matrix containing an active substance. The method is characterized in that a copolymer is used that is composed of 20 to 33 % by weight of methacrylic acid, 5 to 30 % by weight of Me acrylate, 20 to 40 % by weight of Et
acrylate, and more than 10 to 30 % by weight of Bu methacrylate and optionally 0 to 10 % by weight of addnl. vinylically copolymerizable monomers, with the proviso that the glass temperature of the copolymer is 55 to 70° according to ISO 11357-2, item 3.3.3. The invention also relates to the dosage form produced according to the invention, to the copolymer and to the use thereof. Thus a copolymer composed of (weight/weight%): methacrylic acid 30; methylacrylate 20; ethylacrylate 30 and butylmethacrylate 20 was used for the coating of quinidine sulfate; 469.7 g of the emulsion copolymerizate was mixed with 8.5 g polysorbate 80 (33% aqueous solution), 7.0 g glycerol monostearate and 268.7 g water. The coating suspension was applied in a spray-coating apparatus onto 200 g quinidine sulfate cores to result a 6.0 mg/cm2 coating.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

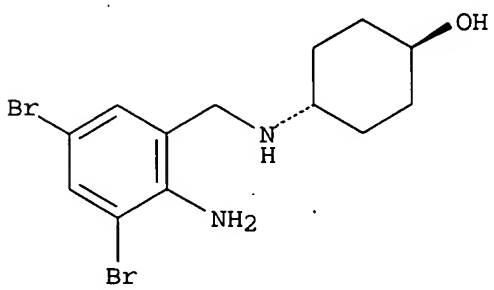
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:625142 CAPLUS
DOCUMENT NUMBER: 141:134112
TITLE: Drug combination comprising alpha-**lipoic acid**, ambroxol and/or inhibitors of the angiotensin converting enzyme (ACE) for use in the prevention and treatment of neurodegenerative diseases
INVENTOR(S): Ansorge, Siegfried; Roehnert, Peter; Striggow, Frank; Taeger, Michael; Reymann, Klaus; Schroeder, Ulrich
PATENT ASSIGNEE(S): Keyneurotek A.-G., Germany; IMTM G.m.b.H.
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1442743	A1	20040804	EP 2004-1224	20040121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
DE 10303229	A1	20040826	DE 2003-10303229	20030128
CA 2455246	AA	20040728	CA 2004-2455246	20040116
US 2004219207	A1	20041104	US 2004-764676	20040126
JP 2004307467	A2	20041104	JP 2004-18916	20040127
PRIORITY APPLN. INFO.:			DE 2003-10303229 A	20030128

IT **18683-91-5**, Ambroxol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combination comprising alpha-**lipoic acid**, ambroxol and/or inhibitors of angiotensin converting enzyme (ACE) for use in prevention and treatment of neurodegenerative diseases)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

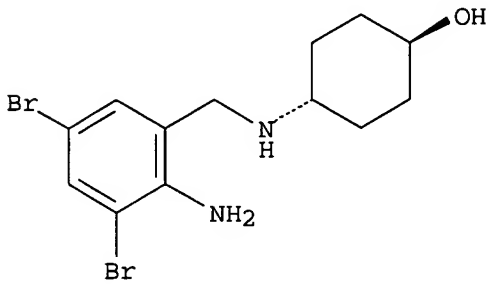


AB The invention concerns a drug combination comprising alpha-**lipoic acid**, ambroxol and/or inhibitors of the angiotensin converting enzyme (ACE), e.g. enalapril, for use in the prevention and treatment of neurodegenerative diseases. The activity of the combination is based on the fact that damaged neuronal cells exhibit fewer thiol groups than other CNS cells and that the drug combination is able to diminish the damage by

40-45 %. A typical combination that was used for tissue culture expts. included 10 μg/mL α- **lipoic acid**, 10 μM ambroxol and 20 μg/mL enalapril.

L4 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:443865 CAPLUS
DOCUMENT NUMBER: 141:186294
TITLE: Effect of paraquat intoxication and ambroxol treatment on hydrogen peroxide production and **lipid** peroxidation in selected organs of rat
AUTHOR(S): Anguelov, Anguel; Chichovska, Maria
CORPORATE SOURCE: Regional Veterinary Station, Plovdiv, Bulg.
SOURCE: Veterinarski Arhiv (2004), 74(2), 141-155
CODEN: VEARA6; ISSN: 0372-5480
PUBLISHER: University of Zagreb, Faculty of Veterinary Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **18683-91-5**, Ambroxol
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(paraquat intoxication and ambroxol treatment effect on hydrogen peroxide production and **lipid** peroxidn. in selected organs of rat)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



AB Expts. with the herbicide paraquat were carried out on Wistar rats. The concentration of hydrogen peroxide (H2O2) and various **lipid** peroxidn. products (LPP), such as conjugated dienes (CD), **lipid** peroxides (LH), malonyl-dialdehyde (MDA) and Schiff bases in selected organs of the rat given a single intra-peritoneal dose of 35 mg/kg-1 paraquat was examined The influence of a mucolytic and probably antioxidant drug, ambroxol, on paraquat-induced changes in the concentration of H2O2 and LPP was also examined Paraquat increased the pulmonic, cardiac and hepatic concentration of H2O2, CD, LH and MDA approx. fourfold. Although the dose of paraquat was nearly twice the LD50 dose, it did not noticeably increase the concentration of these substances in the kidney. Ambroxol alleviated the increase of H2O2 in the liver but did not reduce the concentration of CD, LH and CD. The results indicate that ambroxol did not alleviate the increase the pulmonic concentration of H2O2, but protected the increase in the concentration of CD and MDA. Moreover, the drug administration alone induced **lipid** peroxidn. in the liver. Ambroxol alone acts as a pro-oxidant.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

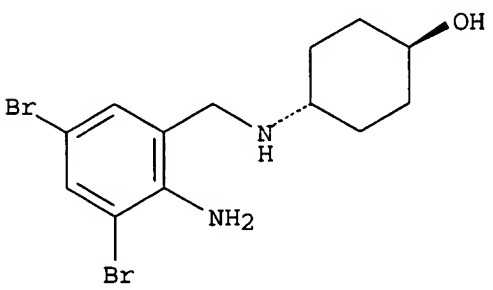
L4 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:696722 CAPLUS
DOCUMENT NUMBER: 139:219350
TITLE: Pharmaceutical dosage forms coated with and acrylic copolymers
INVENTOR(S): Petereit, Hans-Ulrich; Suefke, Thomas; Meier, Christian; Schnabel, Michael; Blesing, Ingrid; Grimm, Stefan
PATENT ASSIGNEE(S): Roehm G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072087	A1	20030904	WO 2003-EP934	20030130
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10208335	A1	20030904	DE 2002-10208335	20020227
CA 2476972	AA	20030904	CA 2003-2476972	20030130
EP 1478352	A1	20041124	EP 2003-711870	20030130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008006	A	20050104	BR 2003-8006	20030130

PRIORITY APPLN. INFO.:
DE 2002-10208335 A 20020227
WO 2003-EP934 W 20030130

IT **18683-91-5**, Ambroxol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical dosage forms coated with and acrylic copolymers)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



AB The invention relates to a method for producing a pharmaceutical dosage form as tablets, pellets and/or in the form of an active ingredient-containing matrix, whereby the tablets, pellets and/or active ingredient-containing matrix contain a pharmaceutical active ingredient and a copolymer serving as a coating agent and/or binding agent, and optionally contain a core and pharmaceutically common additives. According to the invention, the copolymer, the pharmaceutical active ingredient, the optionally present core and/or the pharmaceutically common additives are processed using known techniques by melting, injection molding, extrusion, wet granulation, casting, dipping, spreading out, spraying on, or pressing to form tablets, pellets and/or an active ingredient-containing matrix. The inventive method is characterized in that a copolymer is used that consists of 20 to 34 weight % methacrylic acid, 20 to 69 weight % methylacrylate and 0 to 40 weight % ethylacrylate and, optionally, of 0 to 10 weight % of addnl. vinylically copolymerizable monomers with the provision that the glass transition temperature of the copolymer is no higher than 60° according to ISO 11357-2, Item 3.3.3. The invention also relates to the pharmaceutical dosage form produced according to this method, said copolymer and the use thereof. Thus a copolymer was prepared using the monomers: Me acrylate 40; Et acrylate 30; methacrylic acid 30. An emulsion polymerizate containing 30% of the copolymer was mixed with 0.85% sodium lauryl sulfate (in relation to the copolymer); the fluid was dried to a film; the film was soluble in an artificial intestinal juice at pH 6.8.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:927238 CAPLUS
DOCUMENT NUMBER: 138:323
TITLE: Medicament containing an effector of glutathione metabolism together with α- **lipoic acid** for use within the framework of artificial kidney therapy
INVENTOR(S): Tager, Michael; Ansorge, Siegfried; Fries, Gerhard; Koegst, Dieter
PATENT ASSIGNEE(S): Serumwerk Bernburg AG, Germany
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096414	A1	20021205	WO 2002-DE1991	20020524
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10125883	A1	20021212	DE 2001-10125883	20010528

EP 1392285	A1	20040303	EP 2002-747189		20020524
EP 1392285	B1	20050209			
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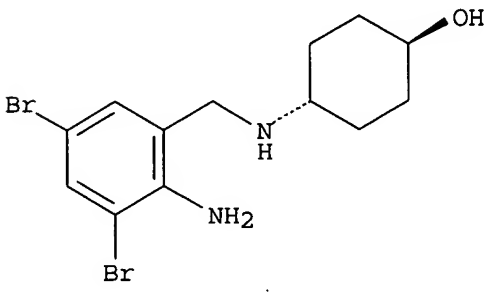
BR 2002009732	A	20040914	BR 2002-9732		20020524
JP 2004535410	T2	20041125	JP 2002-592924		20020524
AT 288750	E	20050215	AT 2002-747189		20020524
US 2004127550	A1	20040701	US 2003-479080		20031126
PRIORITY APPLN. INFO.:			DE 2001-10125883	A	20010528
			WO 2002-DE1991	W	20020524

IT **18683-91-5**, Ambroxol **18683-91-5D**, Ambroxol, prodrug derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glutathione metabolism effector and α- **lipoic acid** for use within framework of artificial kidney therapy)

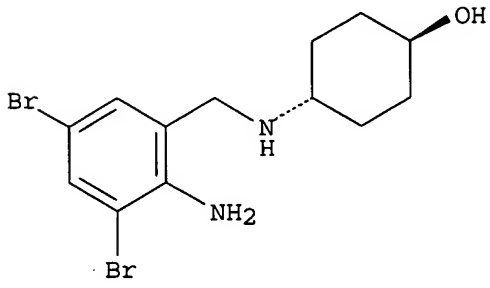
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



AB The invention relates to a medicament containing an effector of the glutathione metabolism together with α- **lipoic acid**, its salts and/or prodrugs, as a combined preparation for the simultaneous, sep. or time-controlled treatment of a defective thiol-disulfide status in artificial kidney therapy in which clin. characteristics indicate a disorder of the thiol-disulfide status of immunocytes. The correction of defective thiol metabolism is of fundamental importance in basic therapy for

large number of diseases of different origins, in particular, however, in circumstances requiring artificial kidney therapy.

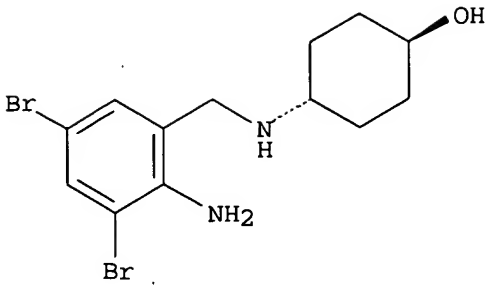
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:927223 CAPLUS
DOCUMENT NUMBER: 138:330
TITLE: Medicament containing an effector of glutathione metabolism and α- **lipoic acid** for treating diabetes mellitus
INVENTOR(S): Tager, Michael; Ansorge, Siegfried; Fries, Gerhard; Koegst, Dieter
PATENT ASSIGNEE(S): Esparma GmbH, Germany; IMTM GmbH
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096398	A2	20021205	WO 2002-EP5811	20020527
WO 2002096398	A3	20030227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10125882	A1	20021212	DE 2001-10125882	20010528
EP 1392288	A2	20040303	EP 2002-774028	20020527
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004531567	T2	20041014	JP 2002-592909	20020527
US 2004138311	A1	20040715	US 2003-478174	20031118
PRIORITY APPLN. INFO.:			DE 2001-10125882 A	20010528
			WO 2002-EP5811 W	20020527

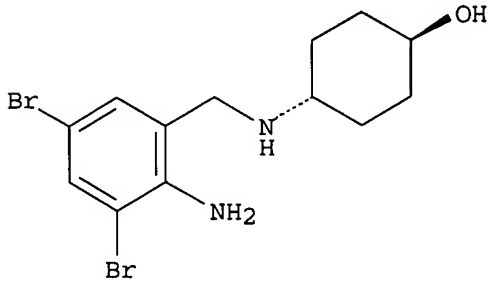
IT **18683-91-5**, Ambroxol **18683-91-5D**, Ambroxol, prodrug derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glutathione metabolism effector and α- **lipoic acid** for treating diabetes mellitus)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

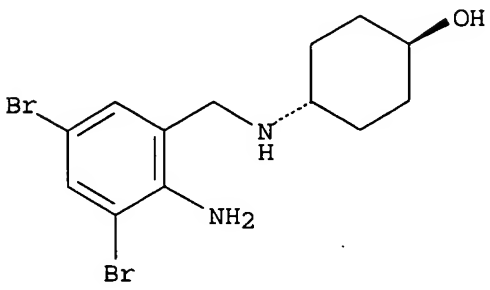


AB The invention provides a medicament containing an effector of glutathione metabolism together with α- **lipoic acid** for treating diabetes mellitus. The medicament enables disturbances of thiol-disulfide status or those that occur e.g. in diabetes mellitus to be treated simultaneously, sep., or in a temporally-graduated manner.

L4 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:719652 CAPLUS
DOCUMENT NUMBER: 137:482
TITLE: Protective effect of ambroxol against lung damage in chronically hypoxic rats
AUTHOR(S): Kuang, Tuguang; Zhang, Hongyu; Pang, Baosen; Niu, Shujie; Weng, Xinzhi; Zhang, Jie; Mao, Yanling; Huang, Xiuxia
CORPORATE SOURCE: Beijing Chaoyang Hospital, Beijing Institute of Respiratory Medicine, Beijing, 100020, Peop. Rep. China
SOURCE: Zhongguo Bingli Shengli Zazhi (2001), 17(8), 759-761
CODEN: ZBSZEB; ISSN: 1000-4718
PUBLISHER: Jinan Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
IT **18683-91-5**, Ambroxol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective effect of ambroxol against lung damage in chronically hypoxic rats)
RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

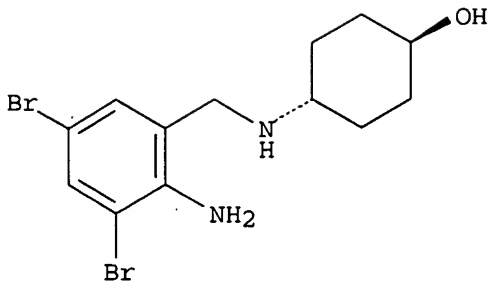
Relative stereochemistry.



AB The effect of ambroxol on pulmonary and vascular injury in chronically hypoxic rats was studied. Thirty-six male Wistar rats were randomly divided into 3 groups: normal control, chronically intermittent hypoxia (CIH) and CIH + ambroxol precaution group (AP). The mean pulmonary artery pressure (PAPM) and the levels of superoxide dismutase (SOD) and nitric oxide (NO), **lipid** peroxide in plasma and in the lung homogenate were determined The SOD and NO levels in plasma and lung homogenate in CIH group were significantly lower than that of normal control and AP group ($P < 0.01$), but the LPO level was significantly higher ($P < 0.01$). PAPM in AP group was significantly lower than that of CIH group ($P < 0.01$); the damage of pulmonary artery smooth muscle cells and extra cell matrix of AP group were much slighter than that of CIH group. Thus, ambroxol might be an effective protector in chronically hypoxic rats.

L4 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:752687 CAPLUS
DOCUMENT NUMBER: 133:305464
TITLE: Antioxidant activity of mucolytics
AUTHOR(S): Strapkova, Anna
CORPORATE SOURCE: Ustav farmakologie, Jeseniova Lek. Fakulta, Univ. Komenskeho, Martin, 037 53, Slovakia
SOURCE: Farmaceuticky Obzor (2000), 69(8-9), 231-235
CODEN: FAOBAS; ISSN: 0014-8172
PUBLISHER: Vydavatelstvo Zdravotnickej Literatury HERBA
DOCUMENT TYPE: Journal
LANGUAGE: Slovak
IT **18683-91-5**, Ambroxol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(ambroxol and N-acetylcysteine mucolytic agents effects on trachea and lung smooth muscle reactivity in guinea pigs and relation to antioxidant activity)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



AB The effects of the mucolytic agents N-acetylcysteine and ambroxol were studied in guinea pigs with respiratory airways reactivity increased by toluene as an agent inducing cell membrane **lipid** peroxidn. The in vitro reactivity of tracheal and lung tissue smooth muscles to histamine was evaluated after animal pretreatment with N-acetylcysteine s.c. or ambroxol i.p. (300 mg/kg) and toluene exposure. The mucolytics were tested also via the inhalation route. No significant changes in the tracheal smooth muscle reactivity were found in the pretreated animals compared to controls. Ambroxol and N-acetylcysteine decreased the lung tissue reactivity. The ambroxol effects were overall stronger than those of N-acetylcysteine. Ambroxol i.p. pretreatment was more effective than the inhalation pretreatment, while N-acetylcysteine was more effective after the inhalation use. The protective effects of mucolytics in the lung tissue may be related to their antioxidant activity, different antioxidant mechanisms, evoked reactivity changes, or other mechanisms.

L4 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:456858 CAPLUS
DOCUMENT NUMBER: 133:94512
TITLE: Improved formulation for topical non-invasive application in vivo
INVENTOR(S): Cevc, Gregor
PATENT ASSIGNEE(S): Idea Innovative Dermale Applikationen G.m.b.H., Germany
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038653	A1	20000706	WO 1998-EP8421	19981223
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356080	AA	20000706	CA 1998-2356080	19981223
AU 9925137	A1	20000731	AU 1999-25137	19981223
AU 770803	B2	20040304		
EP 1140021	A1	20011010	EP 1998-966846	19981223

EP 1140021	B1	20040804			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
BR 9816113	A	20011023	BR 1998-16113		19981223
JP 2002533379	T2	20021008	JP 2000-590607		19981223
EE 200100342	A	20021015	EE 2001-200100342		19981223
RU 2207844	C2	20030710	RU 2001-120008		19981223
AT 272391	E	20040815	AT 1998-966846		19981223
HR 2001000309	A1	20020630	HR 2001-309		20010502
NO 2001003164	A	20010822	NO 2001-3164		20010622
US 2002064524	A1	20020530	US 2001-887493		20010622
PRIORITY APPLN. INFO.:			WO 1998-EP8421	A	19981223

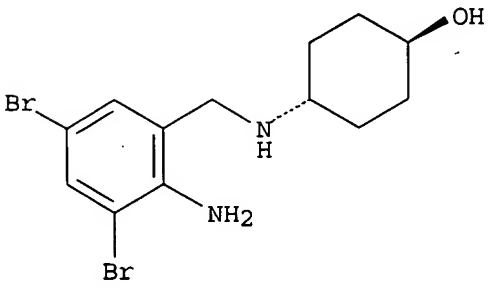
OTHER SOURCE(S): MARPAT 133:94512

IT **18683-91-5**, Ambroxol
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(penetrating formulation for topical non-invasive application in vivo)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



AB A formulation comprises mol. arrangements capable of penetrating pores in a barrier, owing to penetrant adaptability, despite the fact that the average diameter of the pores is smaller than the average penetrant diameter, provided that the penetrants can transport agents or cause permeation through the pores after penetrants have entered pores. The formulation comprises at least 1 consistency builder in an amount that increases the formulation to maximally 5 Nm/s so that spreading over is enabled. The formulation also contains 1 antioxidant in an amount that reduces the increase of oxidation index to <100% per 6 mo and/or at least 1 microbicide in an amount that reduces the bacterial count of 1 million germs added/g of total mass of the formulation to <100 in the case of aerobic bacteria, to <10 in the case of entero-bacteria, and to <1 in the case of Pseudomonas aeruginosa or Staphilococcus aureus, after a period of 4 days. Thus, a composition contained soybean phosphatidylcholine 347, Tween-80 623, sodium dodecyl sulfate 30, benzyl alc. 50, clobetasol 17-propionate 25 and pH 6.5 50 mM phosphate buffer 9000 mg.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:742423 CAPLUS

DOCUMENT NUMBER: 126:27867

TITLE: Effect of paraquat intoxication and ambroxol treatment

on hydrogen peroxide production and **lipid** peroxidation in selected organs of rat

AUTHOR(S): Piotrowski, Wojciech Jerzy; Pietras, Tadeusz; Kurmanowska, Zofia; Nowak, Dariusz; Marczak, Jerzy; Marks-Konczalik, Joanna; Mazerant, Piotr

CORPORATE SOURCE: Dep. Pneumol. Allergy, Univ. Lodz, Pol.

SOURCE: Journal of Applied Toxicology (1996), 16(6), 501-507
CODEN: JJATDK; ISSN: 0260-437X

PUBLISHER: Wiley

DOCUMENT TYPE: Journal

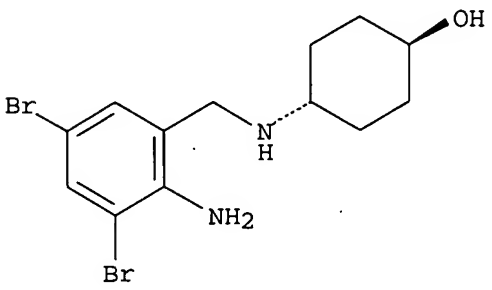
LANGUAGE: English

IT **18683-91-5**, Ambroxol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(paraquat intoxication and ambroxol treatment effect on hydrogen peroxide production and **lipid** peroxidn. in selected organs)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



AB In the present study we examined the concentration of hydrogen peroxide (H2O2) and various **lipid** peroxidn. products (LPP) such as conjugated dienes (CD), **lipid** hydroperoxides (LH), malonyldialdihyde (MDA) and Schiff bases in selected organs of the rat given a single i.p. dose 35 mg kg-1 paraquat (Pq). We also evaluated the influence of a mucolytic and probably antioxidant drug, ambroxol, on Pq-induced changes in the concentration of H2O2 and LPP. Paraquat increased the hepatic concentration of H2O2, CD, LH and MDA by approx. fourfold. Though the dose of Pq was nearly twice the LD50 dose, we did not notice any changes in the concentration of these substances in the critical organ, lung or heart and kidney. Ambroxol alleviated the increase of H2O2 in the liver but did not reduce the concentration of LPP. Moreover, the drug administered alone induced **lipid** peroxidn. in the liver. Our results indicate that Pq does not induce H2O2 production and **lipid** peroxidn. in the lung but it increases the concentration of H2O2 and LPP in the liver. Ambroxol inhibits the Pq-induced increase in the concentration of H2O2 in the liver without protecting it against **lipid** peroxidn. Moreover, the drug alone may act as a pro-oxidant.

L4 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

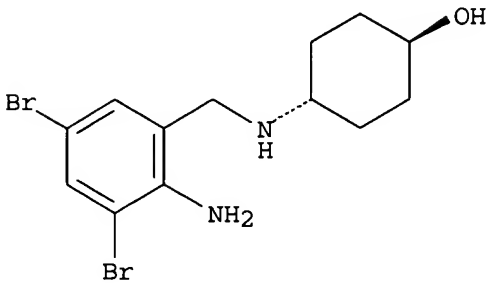
ACCESSION NUMBER: 1995:835170 CAPLUS

DOCUMENT NUMBER: 123:246257

TITLE: Ambroxol inhibits doxorubicin-induced **lipid** peroxidation in heart of mice

AUTHOR(S): Nowak, Dariusz; Pierscinski, Grzegorz; Drzewoski, Jozef
CORPORATE SOURCE: Dep. of Pneumonology and Allergology, Medical Univ. of Lodz, Lodz, Pol.
SOURCE: Free Radical Biology & Medicine (1995), 19(5), 659-63
CODEN: FRBMEH; ISSN: 0891-5849
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **18683-91-5**, Ambroxol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ambroxol inhibits doxorubicin-induced **lipid** peroxidn. in heart of mice)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

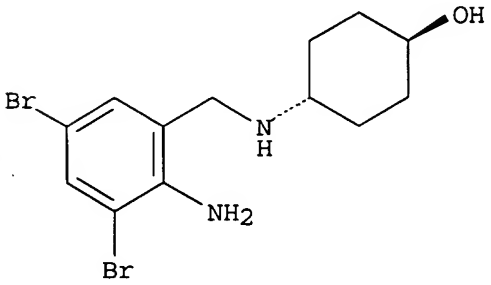


AB A single i.v. injection of doxorubicin (DOX, 30 mg/kg body weight) caused a significant rise in the content of **lipid** peroxidn. products in hearts of mice. The concentration of conjugated dienes (CD) and malondialdehyde (MDA) found 24 h after injection of DOX increased about 1.8- and 2.4-fold and reached values of 11.31 A233/g and 3.72 μmol/g. resp. The same dose of 4'-epi-doxorubicin (EPI), a less cardiotoxin epimer of DOX, increased only the heart level of MDA. Both anthracyclines were not able to induce increased formation of CD in murine liver and lungs. Ambroxol, an expectorant drug which possesses the ability to scavenge hydroxyl radicals, injected i.v. (70 mg/kg) 30 min prior to DOX, completely abolished the rise in heart content of CD and MDA. The heart levels of CD and MDA in animals treated with ambroxol and DOX were 3 and 2.7 times lower than those observed in mice treated with water and DOX, resp. Ambroxol had no effect on DOX- and EPI-induced formation of MDA in the lungs. The results indicate that DOX is a more powerful inducer of **lipid** peroxidn. in the heart than EPI and ambroxol may be useful for preventing **lipid** peroxidn. in the heart caused by DOX.

L4 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:215096 CAPLUS
DOCUMENT NUMBER: 122:742
TITLE: Protective effect of ambroxol against heat- and hydrogen peroxide-induced damage to lung **lipids** in mice
AUTHOR(S): Nowak, D.; Antczak, A.; Pietras, T.; Bialasiewicz, P.;

Krol, M.
CORPORATE SOURCE: Dept. of Pneumology and Allergology, Medical University of Lodz, Lodz, 90-153, Pol.
SOURCE: European Respiratory Journal (1994), 7(9), 1629-34
CODEN: ERJOEI; ISSN: 0903-1936
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **18683-91-5**, Ambroxol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antioxidant ambroxol protection against heat- and hydrogen peroxide-induced lung **lipid** peroxidn.)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

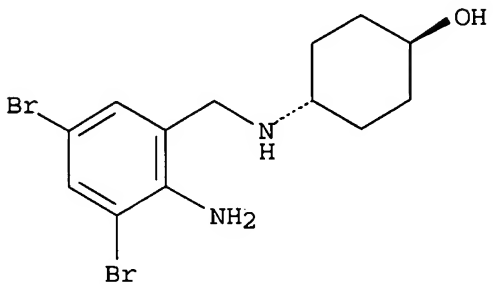


AB We wanted to determine whether ambroxol, a drug which stimulates the release of surfactant by type II pneumocytes, can protect lung **lipids** from peroxidative damage in mice. Animals were injected i.p. with ambroxol, 0.169 mmol·kg-1, or 1 mL buffer once a day for three consecutive days. **Lipid** peroxidn. was then induced in lung homogenates either by means of heat, 50°C, or H2O2, 10 mmol·l-1. The lung homogenates from ambroxol-treated animals revealed decreased **lipid** peroxidn. in response to both stimuli. The heat- and H2O2-induced generation of conjugated dienes (a first **lipid** peroxidn. product) in ambroxol-treated lung homogenates was 3.7 and 3.1 fold lower than in the lungs from buffer-injected mice. Ambroxol, as an inhibitor of heat- and H2O2-induced **lipid** peroxidn., was equipotent to and stronger than the two antioxidants, N-acetylcysteine and methionine, resp. Ambroxol was not able to protect heart and liver **lipids.** These results suggest that ambroxol can sufficiently enhance the antioxidant defense in lung tissue and can act as a lung **lipid** antioxidant.

L4 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:426810 CAPLUS
DOCUMENT NUMBER: 121:26810
TITLE: Antioxidant properties of Ambroxol
AUTHOR(S): Nowak, Dariusz; Antczak, Adam; Krol, Maciej; Bialasiewicz, Piotr; Pietras, Tadeusz
CORPORATE SOURCE: Dep. Pneumonology Allergology, Med. Univ. Lodz, Lodz, Pol.
SOURCE: Free Radical Biology & Medicine (1994), 16(4), 517-22
CODEN: FRBMEH; ISSN: 0891-5849

DOCUMENT TYPE: Journal
LANGUAGE: English
IT **18683-91-5**, Ambroxol
RL: BIOL (Biological study)
(antioxidant activity of, scavenging of reactive oxygen species in relation to)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

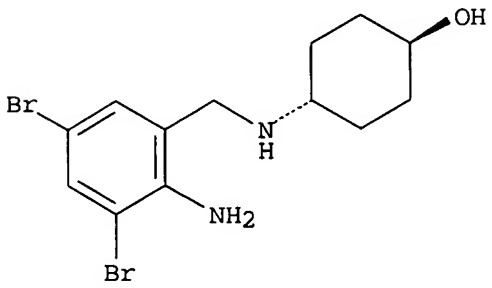


AB The authors tested whether Ambroxol, a drug which stimulates the release of surfactant by pneumocytes type II, may also possess antioxidant properties. To assess the reactivity of Ambroxol with reactive oxygen species, the authors analyzed its ability to decompose hydrogen peroxide (H2O2) and to inhibit the superoxide (O2•-)-dependent autoxidn. of pyrogallol, hydroxyl radical (•OH)-mediated deoxyribse oxidation, and hypochlorous acid (HClO)-induced chlorination of monochlorodimedon. Ambroxol was found to be a sufficient scavenger of HClO and •OH and also revealed the capacity to decompose H2O2. At concns. of 25 and 70 μM, it inhibited HClO-induced chlorination of monochlorodimedon by 22 ± 13 and 59 ± 14%, resp. Similarly, at concns. of 1, 2, and 10 mM, Ambroxol decreased •OH-mediated deoxyribose oxidation by 47 ± 11, 75 ± 9, and 89 ± 4%. In addition, at concns. of 1 to 5 mM, it completely protected linoleic acid from •OH-induced peroxidative damage. Ambroxol had a weak effect on O2•--dependent autoxidn. of pyrogallol. The authors' results indicate that Ambroxol has antioxidant activity, which may have clin. significance in protecting lung tissue from oxidant-induced injury.

L4 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:95731 CAPLUS
DOCUMENT NUMBER: 120:95731
TITLE: Ambroxol inhibits endotoxin-induced **lipid** peroxidation in mice
AUTHOR(S): Nowak, Dariusz; Pietras, Tadeusz; Antczak, Adam; Krol, Maciej; Piasecka, Grazyna
CORPORATE SOURCE: Dep. Pneumonol. Allergol., Med. Acad., Lodz, 90-153, Pol.
SOURCE: Polish Journal of Pharmacology (1993), 45(3), 317-22
CODEN: PJPAE3; ISSN: 1230-6002
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **18683-91-5**, Ambroxol
RL: BIOL (Biological study)
(**lipid** peroxidn. induced by endotoxin inhibition by, in heart

and lung)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

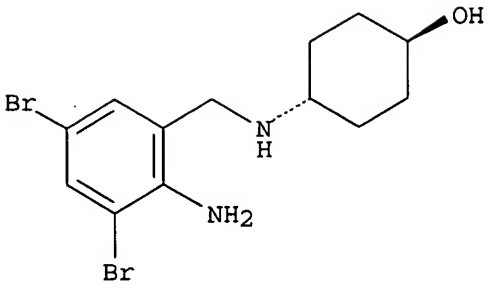
Relative stereochemistry.



AB Administration of ambroxol (70 mg/kg i.p.) once a day for 3 days protected lung and heart **lipids** from lipopolysaccharide (LPS, 17 mg/kg) - induced oxidative stress in mice. Ambroxol as a **lipid** peroxidn. inhibitor was almost as active as an equivalent dose of N-acetylcysteine (27.6 mg/kg), a well known antioxidant. The lung and heart levels of conjugated dienes in animals pretreated with ambroxol were 3.3- and 1.7-times lower (and) than those observed in the control group which received only buffer and subsequently LPS. These results indicate that ambroxol can sufficiently inhibit the harmful process of **lipid** peroxidn. in vivo.

L4 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:462779 CAPLUS
DOCUMENT NUMBER: 119:62779
TITLE: The influence of Ambroxol on peroxidative processes in lung and plasma in dogs after pulmonectomy
AUTHOR(S): Jablonka, Stanislaw; Ledwozyw, Andrzej; Kadziolka, Wojciech; Jablonka, Andrzej; Nestorowicz, Andrzej
CORPORATE SOURCE: Dep. Thoracic Cardiac Surg., Medical Acad., Lublin, Pol.
SOURCE: Archivum Veterinarium Polonicum (1992), 32(1-2), 57-66
CODEN: AVPOEW; ISSN: 0079-3647
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **18683-91-5**, Ambroxol
RL: BIOL (Biological study)
(peroxidn. in blood plasma and lung response to)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

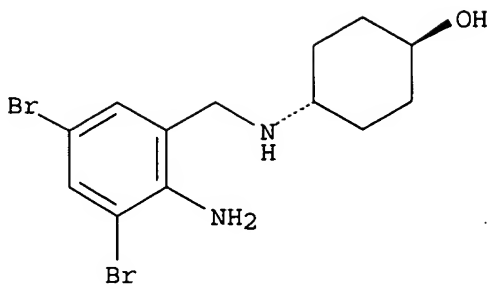
Relative stereochemistry.



AB The purpose of the studies was to determine the effect of Ambroxol on the activity of antioxidant enzymes and on the glutathione level as well as the intensity of the peroxidative processes in the lung tissue, alveolar macrophages and plasma in dogs after unilateral pulmonectomy. On the 2nd and 6th day after the surgery the activity of antioxidant enzymes and the glutathione level were studied in the remaining lung. The levels of the **lipid** peroxidn. products were determined in the analogous system. In both examined groups the increase in the antioxidant enzyme activity and the **lipid** peroxidn. product levels was observed in the remaining lung after the surgery. In Ambroxol-treated animals the statistically significant increase in the antioxidant enzyme activity was noted while the intensity of peroxidative processes was found to be lower. This fact may suggest that Ambroxol stimulates the resistance of the lung tissue to the free radical activity and inhibits the lung peroxidative processes in dogs after pulmonectomy.

L4 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:175674 CAPLUS
DOCUMENT NUMBER: 118:175674
TITLE: Effect of the loading method on the drug release from crosslinked carboxymethyl cellulose beads
AUTHOR(S): Iannuccelli, Valentina; Forni, Flavio; Vandelli, Maria Angela; Bernabei, Maria Teresa
CORPORATE SOURCE: Dep. Pharm. Sci, Univ. Modena, Modena, Italy
SOURCE: Journal of Controlled Release (1993), 23(1), 13-20
CODEN: JCREEC; ISSN: 0168-3659
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **23828-92-4**, Ambroxol hydrochloride
RL: BIOL (Biological study)
(release of, from crosslinked CM-cellulose beads, loading method effect on)
RN 23828-92-4 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

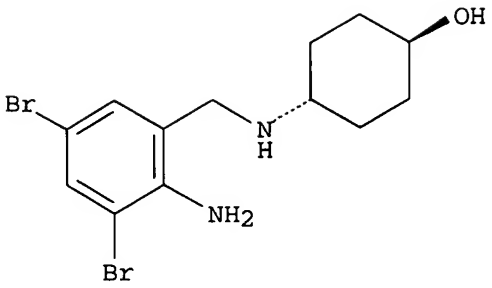


● HCl

AB Spherical matrixes (beads) of crosslinked CM-cellulose were prepared by the in-**lipid** curing coating process using AlCl3 as curing agent (crosslinker). The loading process was carried out either by adding the drug to the polymer solns. before the extrusion process or be swelling the crosslinked beads in a drug solution The energy dispersive x-ray anal. showed a homogeneous distribution of both the drug concentration and crosslinking
d. in the network regardless to the loading procedure. When the loading process was carried out before the extrusion process, a residual amount of AlCl3 remained in the beads. The effects of the residual amount of AlCl3 on the matrix swelling and drug release processes were analyzed.

L4 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:160858 CAPLUS
DOCUMENT NUMBER: 118:160858
TITLE: The effect of ambroxol on peroxidative processes in dog lung mitochondria
AUTHOR(S): Ledwozyw, Andrzej; Jablonka, Stanislaw; Tusinska, Elzbieta
CORPORATE SOURCE: Zakl. Patofizjol., Akad. Roln., Lublin, Pol.
SOURCE: Polskie Archiwum Weterynaryjne (1991), 31(3-4), 105-13
CODEN: PARWAC; ISSN: 0079-3647
DOCUMENT TYPE: Journal
LANGUAGE: Polish
IT **18683-91-5**, Ambroxol
RL: BIOL (Biological study)
(lung **lipid** peroxidn. inhibition by, phospholipids in)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

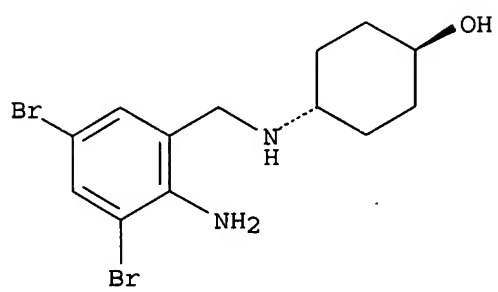
Relative stereochemistry.



AB The influence of ambroxol on the Fe3+/ADP/dihydroxyfumarate-induced peroxidn. of mitochondrial **lipids** in the dog lung was investigated. Changes in mitochondrial **lipid** composition included decreases in phosphatidylcholine and phosphatidylethanolamine content and increases in lysophosphoglycride content. Addition of ambroxol (5 and 10 mM) to the incubation medium decreased these changes in a concentration-dependent manner. The malondialdehyde production was greatly reduced in the presence of ambroxol. The mode of ambroxol action was comparable to that of other free radical scavengers.

L4 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:622628 CAPLUS
DOCUMENT NUMBER: 115:222628
TITLE: High-performance liquid chromatography post-column derivatization with fluorescence detection to study the influence of ambroxol on dipalmitoylphosphatidylcholine levels in rabbit eustachian tube washings
AUTHOR(S): Kitsos, M.; Gandini, C.; Massolini, G.; De Lorenzi, E.; Caccialanza, G.
CORPORATE SOURCE: Dep. Pharm. Chem., Pavia, Italy
SOURCE: Journal of Chromatography (1991), 553(1-2), 1-6
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **18683-91-5**, Ambroxol
RL: BIOL (Biological study)
(dipalmitoylphosphatidylcholine in eustachian tube washings response to)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

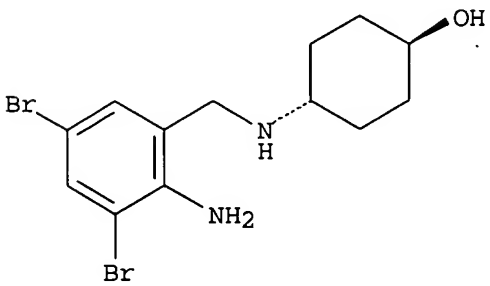
Relative stereochemistry.



AB In this work an appropriate HPLC method was set up to guarantee specificity, sensitivity, precision and accuracy in analyzing dipalmitoylphosphatidylcholine (DPPC) in rabbit eustachian tube washings, as well as to determine its varying levels after administration of ambroxol chloride. The procedure is based on a post-column derivatization with fluorescence detection using 1,6-diphenyl-1,3,5-hexatriene which exhibits increased fluorescence in a **lipid** environment. DPPC was chromatographed on a Hypersil C18. The mobile phase for the isocratic elution consisted of 40 mmol/L choline chloride in methanol-tetrahydrofuran (97:3). Ambroxol was given to a group of New Zealand white rabbits at a dose of 30 mg/kg. A second group receiving vehicle only acted as controls.

L4 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:509010 CAPLUS
DOCUMENT NUMBER: 111:109010
TITLE: The effects of Oradexon and Ambroxol pretreatment on the oxidative sensitivity of the red blood cells in preterm infants
AUTHOR(S): Novak, Z.; Varga, S. I.; Kovacs, L.; Pal, A.; Pataki, L.; Matkovics, B.
CORPORATE SOURCE: County Munic. Child. Hosp., Szeged, Hung.
SOURCE: Clinica Chimica Acta (1989), 182(3), 241-6
CODEN: CCATAR; ISSN: 0009-8981
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **18683-91-5**, Ambroxol
RL: BIOL (Biological study)
(antioxidant enzymes and **lipid** peroxidn. and lung surfactants of newborn response to maternal administration of)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



AB The antioxidant enzyme activities and **lipid** peroxidn. in the red blood cells of cord blood were investigated and compared at different gestation times in preterm and full-term neonates, with and without pretreatment of the pregnant mothers with Oradexon (dexamethasone) or Ambroxol. Administration of the 2 drugs not only stimulated the lung surfactant system, but also exerted favorable effects on the antioxidant enzyme activities while the **lipid** peroxidn. was decreased.

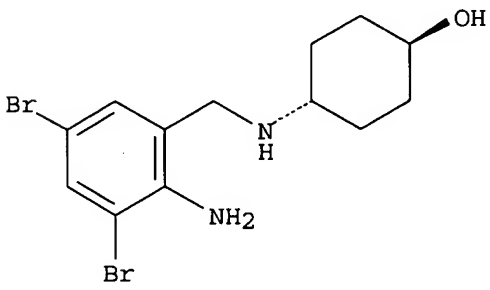
L4 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:137761 CAPLUS

DOCUMENT NUMBER: 108:137761
TITLE: Bioavailability of ambroxol sustained release preparations. Part I: in vitro dissolution studies
AUTHOR(S): Alighieri, T.; Avanessian, S.; Berlini, S.; Bianchi, S. G.; Deluigi, P.; Valducci, R.; Guelen, P. J. M.
CORPORATE SOURCE: Euderma S.r.l., Rimini, Italy
SOURCE: Arzneimittel-Forschung (1988), 38(1), 92-4
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **23828-92-4**, Ambroxol hydrochloride
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(dissoln. of, from sustained-release capsules based on dialyzing membrane)

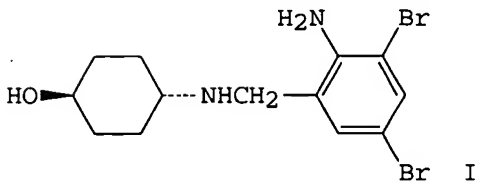
RN 23828-92-4 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

GI



I

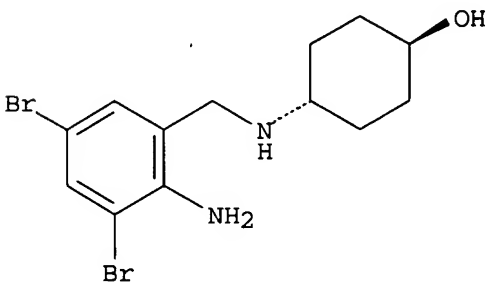
AB The in vitro dissoln. of 2 ambroxol-HCl (I-HCl) sustained-release prepns. (75 mg) and the effect of pH of the dissoln. medium on the dissoln. rates were investigated. The studies were carried out using the USP XXI paddle method. A new I-HCl sustained-release formulation based on a dialyzing membrane for controlled release shows a longer release action as compared to a standard sustained release preparation from com. source which is based on spheroids constituted by a **lipid** matrix. The in vitro release rate of the latter product also appears to be more pH dependent.

L4 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:144014 CAPLUS
DOCUMENT NUMBER: 106:144014
TITLE: Pharmaceutical granulate with delayed release for oral application
INVENTOR(S): Graetzel von Graetz, Jochen; Prochazka, Josef
PATENT ASSIGNEE(S): Heumann, Ludwig, und Co. G.m.b.H., Fed. Rep. Ger.
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3524003	A1	19870108	DE 1985-3524003	19850704
EP 208144	A1	19870114	EP 1986-107700	19860606
EP 208144	B1	19890920		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 46436	E	19891015	AT 1986-107700	19860606
PRIORITY APPLN. INFO.:			DE 1985-3524003 A	19850704
			EP 1986-107700 A	19860606

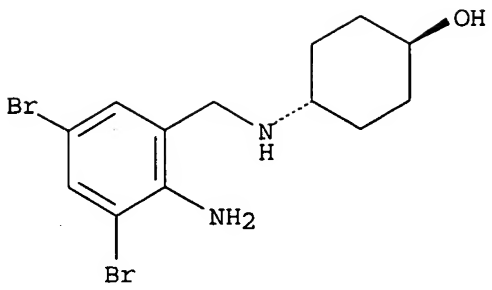
IT **18683-91-5**, Ambroxol **23828-92-4**, Ambroxol hydrochloride
RL: BIOL (Biological study)
(delayed-release compns. for)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 23828-92-4 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

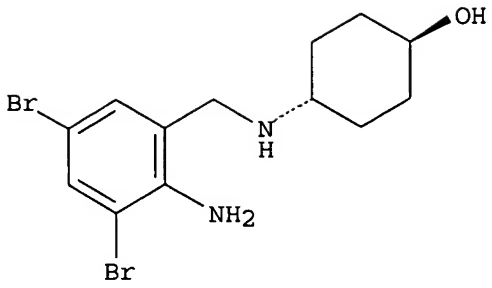


● HCl

AB A pharmaceutical granulate with delayed release contains a **lipid** of m.p. 40-90° 0.2-10, a gastric juice-insol. powdered film former that is soluble in intestinal juice 0.2-10, an active ingredient soluble in gastric juice and difficultly soluble in intestinal juice 1%, and optionally other formulation adjuvants. Finely powdered ambroxol. HCl 75.0, powdered cellulose acetate phthalate 90.0, and montan wax 70.0 g were mixed and pressed through a perforated disk with 1.0 mm. openings, pulverized, and placed in hard gelatin capsules (235 mg/capsule).

L4 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:29491 CAPLUS
DOCUMENT NUMBER: 100:29491
TITLE: The perfused rat lung as a model for studies on the formation of surfactant and the effect of ambroxol on this process
AUTHOR(S): Post, M.; Batenburg, J. J.; Schuurmans, E. A. J. M.; Oldenborg, V.; Van der Molen, A. J.; Van Golde, L. M. G.
CORPORATE SOURCE: Lab. Vet. Biochem., State Univ. Utrecht, Utrecht, 3508 TD, Neth.
SOURCE: Lung (1983), 161(6), 349-59
CODEN: LUNGD9; ISSN: 0341-2040
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **18683-91-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(surfactant phospholipids formation by lung response to)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

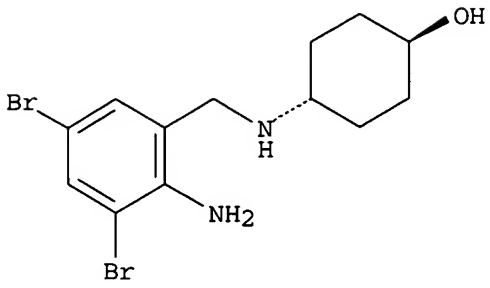
Relative stereochemistry.



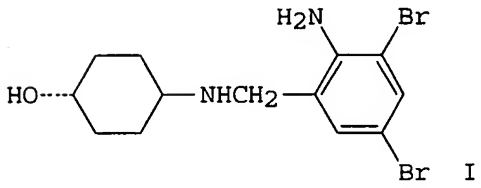
AB The isolated perfused rat lung was used as a model to investigate the synthesis of surfactant phospholipids from various radioactive precursors and the effect of Ambroxol **[18683-91-5]**, a bronchial secretolytic, on this process. Lungs were ventilated and perfused for periods up to 5 h without detectable development of pulmonary edema. The lungs remained metabolically stable during the entire period of perfusion. Both in whole lung tissue and in the surfactant fraction the radioactive substrates were incorporated predominantly into phosphatidylcholine and phosphatidylglycerol. The degree of saturation of labeled phosphatidylcholines synthesized during perfusion with [methyl-14C]choline, D-[U-14C]glucose, [1(3)-3H]glycerol and [1-14C]palmitate was higher in surfactant than in whole lung tissue. A delayed incorporation into surfactant phospholipids was observed for all precursors. Under the conditions employed, glucose carbon was recovered mainly in the glycerol backbone of phosphatidylcholine and phosphatidylglycerol. Compared to glucose, glycerol appeared to be a minor substrate for lung **lipid** formation. If the lungs were perfused after pretreatment of the rats with Ambroxol on 3 consecutive days, the incorporation of labeled choline and glycerol into pulmonary phospholipids was found to be enhanced. This stimulation was more pronounced in the surfactant fraction than in whole lung tissue. The stimulatory effect on the formation of surfactant **lipids** was smaller after pretreatment of the animals with Ambroxol for 1 day. The results of the present study suggest that Ambroxol may specifically stimulate the synthesis of phospholipids in the alveolar type-II cells and that the drug may not only effect the formation but also the secretion of surfactant **lipids** by these cells.

L4 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:605920 CAPLUS
DOCUMENT NUMBER: 99:205920
TITLE: Ambroxol and surfactant secretion. Experimental studies on the incorporation of 3H-palmitate into pulmonary surfactant
AUTHOR(S): Kapanci, Yusuf; Elemer, Gabriella
CORPORATE SOURCE: Fac. Med., Univ. Geneva, Geneva, CH-1211, Switz.
SOURCE: Symposia of the Giovanni Lorenzini Foundation (1983), 16(Pulm. Surfactant Syst.), 263-72
CODEN: SGLFD9; ISSN: 0166-1167
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **18683-91-5**
RL: BIOL (Biological study)
(lung surfactant formation response to)
RN 18683-91-5 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



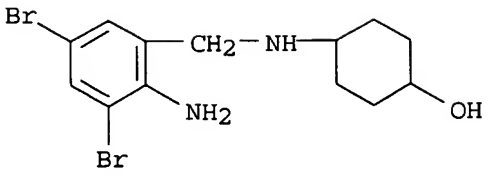
GI



I

AB Ambroxol (I) [**18683-91-5**] was administered to adult rats which were subsequently injected with 3H-labeled palmitate [57-10-3]. One, 4, and 8 h after injection, the localization of the label in lung tissue was evaluated by electron-microscopic autoradiog., using morphometric methods; its incorporation into **lipids** extracted from lung homogenates and alveolar lavage fluids was also measured. Ambroxol stimulated the rate of incorporation of palmitate into lamellar bodies of type II epithelial cells and into the major surfactant **lipid**, phosphatidylcholine.

L4 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1977:50790 CAPLUS
DOCUMENT NUMBER: 86:50790
TITLE: NMR studies on the molecular basis of drug-induced phospholipidosis. II. Interaction between several amphiphilic drugs and phospholipids
AUTHOR(S): Seydel, Joachim K.; Wassermann, Otmar
CORPORATE SOURCE: Dep. Pharm. Chem., Borstel Res. Inst., Borstel, Fed. Rep. Ger.
SOURCE: Biochemical Pharmacology (1976), 25(21), 2357-64
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **36557-04-7**
RL: PRP (Properties)
(interaction of, with phospholipids, phospholipidosis in relation to)
RN 36557-04-7 CAPLUS
CN Cyclohexanol, 4-[[(2-amino-3,5-dibromophenyl)methyl]amino]- (9CI) (CA INDEX NAME)



AB The binding of several amphiphilic drugs with phospholipids was studied by NMR; of the drugs studied, most gave a distinct but quant. different interaction with phosphatidylcholine. Increasing lipophilicity of the drugs was correlated with an increase in binding. The degree of signal broadening in the NMR spectra was determined by the ratio of drug/**lipid** concentration Strong interaction of the drugs occurred with phospholipids, e.g. phosphatidylcholine and phosphatidylethanolamine, whereas less polar **lipids**, e.g. diacylglyerol or digalactosyldiglyceride, showed no interaction. Cholesterol antagonized the phospholipid/drug interaction. Drug-induced phospholipidosis is apparently caused by interaction of the drug with phospholipids so preventing metabolic degradation of the **lipids.**

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	125.13	286.67

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-17.52	-17.52

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